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Document Processing Center (TS-790)
Office of Pollution Prevention and Toxics
Environmental Protection Agency
401 M Street., S.W.
Washington, D.C. 20460
Attn: Section 8(e) Coordinator (CAP Agreement)

Dear Coordinator:

8ECAP-0025

On behalf of the Regulatee and pursuant to Unit II B.1.b. and Unit II C of the 6/28/91CAP Agreement, E.I. Du Pont de Nemours and Co. hereby submits (*in triplicate*) the attached studies. Submission of this information is voluntary and is occasioned by unilateral changes in EPA's standard as to what EPA now considers as reportable information. Regulatee's submission of information is made solely in response to the new EPA §8(e) reporting standards and is not an admission: (1) of TSCA violation or liability; (2) that Regulatee's activities with the study compounds reasonably support a conclusion of substantial health or environmental risk or (3) that the studies themselves reasonably support a conclusion of substantial health or environmental risk.

The "Reporting Guide" creates new TSCA 8(e) reporting criteria which were not previously announced by EPA in its 1978 Statement of Interpretation and Enforcement Policy, 43 Fed Reg 11110 (March 16, 1978). The "Reporting Guide states criteria which expands upon and conflicts with the 1978 Statement of Interpretation. Absent amendment of the Statement of Interpretation, the informal issuance of the "Reporting Guide" raises significant due processes issues and clouds the appropriate reporting standard by which regulated persons can assure TSCA Section 8(e) compliance.

For Regulatee,

CBE CAP

Mark H. Christman
Counsel
Legal D-7158
1007 Market Street
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RECEIVED 4/24/93

## ATTACHMENT 1

Submission of information is made under the 6/28/91 CAP Agreement, Unit II. This submission is made voluntarily and is occasioned by recent changes in EPA's TSCA §8(e) reporting standard; such changes made, for the first time in 1991 and 1992 without prior notice and in violation of Regulatee's constitutional due process rights. Regulatee's submission of information under this changed standard is not a waiver of its due process rights; an admission of TSCA violation or liability, or an admission that Regulatee's activities with the study compounds reasonably support a conclusion of substantial risk to health or to the environment. Regulatee has historically relied in good faith upon the 1978 Statement of Interpretation and Enforcement Policy criteria for determining whether study information is reportable under TSCA §8(e), 43 Fed Reg 11110 (March 16, 1978). EPA has not, to date, amended this Statement of Interpretation.

After CAP registration, EPA provided the Regulatee the June 1, 1991 "TSCA Section 8(e) Reporting Guide". This "Guide" has been further amended by EPA, EPA letter, April 10, 1992. EPA has not indicated that the "Reporting Guide" or the April 1992 amendment supersedes the 1978 Statement of Interpretation. The "Reporting Guide" and April 1992 amendment substantively lowers the Statement of Interpretation 's TSCA §8(e) reporting standard[2]. This is particularly troublesome as the "Reporting Guide" states criteria, applied retroactively, which expands upon and conflicts with the Statement of Interpretation.[3] Absent amendment of the Statement of Interpretation, the informal issuance of the "Reporting Guide" and the April 1992 amendment clouds the appropriate standard by which regulated persons must assess information for purposes of TSCA §8(e).

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[2]In sharp contrast to the Agency's 1977 and 1978 actions to soliciting public comment on the proposed and final §8(e) Policy, EPA has unilaterally pronounced §8(e) substantive reporting criteria in the 1991 Section 8(e) Guide without public notice and comment. See 42 Fed Reg 45362 (9/9/77), "Notification of Substantial Risk under Section 8(e): Proposed Guidance".

[3]A comparison of the 1978 Statement of Interpretation and the 1992 "Reporting Guide" is a appended.

Throughout the CAP, EPA has mischaracterized the 1991 guidance as reflecting "longstanding" EPA policy concerning the standards by which toxicity information should be reviewed for purposes of §8(e) compliance. Regulatee recognizes that experience with the 1978 Statement of Interpretation may cause a review of its criteri. Regulatee supports and has no objection to the Agency's amending reporting criteria *provided that* such amendment is not applied to the regulated community in an unfair way. However, with the unilateral announcement of the CAP under the auspices of an OCM enforcement proceeding, EPA has wrought a terrific unfairness since much of the criteria EPA has espoused in the June 1991 Reporting Guide and in the Agency's April 2, 1992 amendment is new criteria which does not exist in the 1978 Statement of Interpretation and Enforcement Policy.

The following examples of new criteria contained in the "Reporting Guide" that is not contained in the Statement of Interpretation follow:

- o even though EPA expressly disclaims each "status report" as being preliminary evaluations that should not be regarded as final EPA policy or intent[4], the "Reporting Guide" gives the "status reports" great weight as "sound and adequate basis" from which to determine mandatory reporting obligations. ("Guide" at page 20).
- o the "Reporting Guide" contains a matrix that establishes new numerical reporting "cutoff" concentrations for acute lethality information ("Guide" at p. 31). Neither this matrix nor the cutoff values therein are contained in the Statement of Interpretation. The regulated community was not made aware of these cutoff values prior to issuance of the "Reporting Guide" in June, 1991.
- othe "Reporting Guide" states new specific definitional criteria with which the Agency, for the first time, defines as 'distinguishable neurotoxicological effects'; such criteria/guidance not expressed in the 1978 Statement of Interpretation.[5];

- othe "Reporting Guide" provides new review/ reporting criteria for irritation and sensitization studies; such criteria not previously found in the 1978 Statement of Interpretation/Enforcement Policy.
- othe "Reporting Guide" publicizes certain EPA Q/A criteria issued to the Monsanto Co. in 1989 which are not in the Statement of Interpretation; have never been published in the Federal Register or distributed by the EPA to the Regulatee. Such Q/A establishes new reporting criteria not previously found in the 1978 Statement of Interpretation/Enforcement Policy .

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[4]The 'status reports' address the significance, if any, of particular information reported to the Agency, rather than stating EPA's interpretation of §8(e) reporting criteria. In the infrequent instances in which the status reports contain discussion of reportability, the analysis is invariably quite limited, without substantial supporting scientific or legal rationale.

[5] *See, e.g,* 10/2/91 letter from Du Pont to EPA regarding the definition of 'serious and prolonged effects' as this term may relate to transient anesthetic effects observed at lethal levels; 10/1/91 letter from the American Petroleum Institute to EPA regarding clarification of the Reporting Guide criteria.

In discharging its responsibilities, an administrative agency must give the regulated community fair and adequate warning to as what constitutes noncompliance for which penalties may be assessed.

> Among the myriad applications of the due process clause is the fundamental principle that statutes and regulations which purport to govern conduct must give an adequate warning of what they command or forbid.... Even a regulation which governs purely economic or commercial activities, if its violation can engender penalties, must be so framed as to provide a constitutionally adequate warning to those whose activities are governed.

Diebold, Inc. v. Marshall, 585 F.2d 1327, 1335-36 (D.C. Cir. 1978). *See also*, Rollins Environemntal Services (NJ) Inc. v. U.S. Environmental Protection Agency, 937 F. 2d 649 (D.C. Cir. 1991).

While neither the are rules, This principle has been applied to hold that agency 'clarification', such as the Statement of Interpretation, the "Reporting Guide" nor the April 1992 amendments will not applied retroactively.

> ...a federal court will not retroactively apply an unforeseeable interpretation of an administrative regulation to the detriment of a regulated party on the theory that the post hoc interpretation asserted by the Agency is generally consistent with the policies underlying the Agency's regulatory program, when the semantic meaning of the regulations, as previously drafted and construed by the appropriate agency, does not support the interpretation which that agency urges upon the court.

Standard Oil Co. v. Federal Energy Administration, 453 F. Supp. 203, 240 (N.D. Ohio 1978), aff'd sub nom. Standard Oil Co. v. Department of Energy, 596 F.2d 1029 (Em. App. 1978):

The 1978 Statement of Interpretation does not provide adequate notice of, and indeed conflicts with, the Agency's current position at §8(e) requires reporting of all 'positive' toxicological findings without regard to an assessment of their relevance to human health. In accordance with the statute, EPA's 1978 Statement of Interpretation requires the regulated community to use scientific judgment to evaluate the significance of toxicological findings and to determining whether they reasonably support a conclusion of a substantial risk. Part V of the Statement of Interpretation urges persons to consider "the fact or probability" of an effect's occurrence. Similarly, the 1978 Statement of Interpretation stresses that an animal study is reportable only when "it contains reliable evidence ascribing the effect to the chemical." 43 Fed Reg. at 11112. Moreover, EPA's Statement of Interpretation defines the substantiality of risk as a function of both the seriousness of the effect and the probability of its occurrence. 43 Fed Reg 11110 (1978). Earlier Agency interpretation also emphasized the "substantial" nature of a §8(e) determination. See 42 Fed Reg 45362, 45363

(1977). [Section 8(e) findings require "extraordinary exposure to a chemical substance...which critically imperil human health or the environment"].

The recently issued "Reporting Guide" and April 1992 Amendment guidance requires reporting beyond and inconsistent with that required by the Statement of Interpretation. Given the statute and the Statement of Interpretation's explicit focus on substantial human or environmental risk, whether a substance poses a "substantial risk" of injury requires the application of scientific judgment to the available data on a case-by-case basis.

If an overall weight-of-evidence analysis indicates that this classification is unwarranted, reporting should be unnecessary under §8(e) because the available data will not "reasonably support the conclusion" that the chemical presents a substantial risk of serious adverse consequences to human health.

Neither the legislative history of §8(e) nor the plain meaning of the statute support EPA's recent lowering of the reporting threshold that TSCA §8(e) was intended to be a sweeping information gathering mechanism. In introducing the new version of the toxic substances legislation, Representative Eckhart included for the record discussion of the specific changes from the version of H. R. 10318 reported by the Consumer Protection and Finance Subcommittee in December 1975. One of these changes was to modify the standard for reporting under §8(e). The standard in the House version was changed from "causes or contributes to an unreasonable risk" to "causes or significantly contributes to a substantial risk". This particular change was one of several made in TSCA §8 to avoid placing an undue burden on the regulated community. The final changes to focus the scope of Section 8(e) were made in the version reported by the Conference Committee.

The word "substantial" means "considerable in importance, value, degree, amount or extent". Therefore, as generally understood, a "substantial risk" is one which will affect a considerable number of people or portion of the environment, will cause serious injury and is based on reasonably sound scientific analysis or data. Support for the interpretation can be found in a similar provision in the Consumer Product Safety Act. Section 15 of the CPSA defines a "substantial product hazard" to be:

> "a product defect which because of the pattern of defect, the number of defective products distributed in commerce, the severity of the risk, or otherwise, creates a substantial risk of injury to the public."

Similarly, EPA has interpreted the word 'substantial' as a quantitative measurement. Thus, a 'substantial risk' is a risk that can be quantified, *See*, 56 Fed Reg 32292, 32297 (7/15/91). Finally, since information pertinent to the exposure of humans or the environment to chemical substances or mixtures may be obtained by EPA through Sections 8(a) and 8(d) regardless of the degree of potential risk, §8(e) has specialized function. Consequently, information subject to §8(e) reporting should be of a type which would lead a reasonable man to conclude that some type action was required immediately to prevent injury to health or the environment.

# Attachment

***Comparison:***

Reporting triggers found in the 1978 "Statement of Interpretation/ Enforcement Policy",43 Fed Reg 11110 (3/16/78) and the June 1991 *Section 8(e) Guide.*

| TEST TYPE | 1978 POLICY CRITERIA EXIST? | New 1991 GUIDE CRITERIA EXIST? |
|---|---|---|
| **ACUTE LETHALITY** | | |
| Oral | N} | Y} |
| Dermal | N} | Y} |
| Inhalation (Vapors) | }[6] | }[7] |
| aerosol | N} | Y} |
| dusts/ particles | N} | Y} |
| **SKIN IRRITATION** | N | Y[8] |
| **SKIN SENSITIZATION (ANIMALS)** | N | Y[9] |
| **EYE IRRITATION** | N | Y[10] |
| **SUBCHRONIC** (ORAL/DERMAL/INHALATION) | N | Y[11] |
| **REPRODUCTION STUDY** | N | Y[12] |
| **DEVELOPMENTAL TOX** | Y[13] | Y[14] |

[6] 43 Fed Reg at 11114, comment 14:
"This policy statements directs the reporitng of specifiec effects when unknown to the Administrator. Many routine tests are based on a knowledge of toxicity associated with a chemicalL unknown effects occurring during such a range test may have to be reported if they are those of concern tot he Agency and if the information meets the criteria set forth in Parts V and VII."

[7] Guide at pp.22, 29-31.

[8] Guide at pp-34-36.

[9] Guide at pp-34-36.

[10] Guide at pp-34-36.

[11] Guide at pp-22; 36-37.

[12] Guide at pp-22

[13] 43 Fed Reg at 11112
"Birth Defects" listed.

[14] Guide at pp-22

| | | |
|---|---|---|
| **NEUROTOXICITY** | N | Y[15] |
| **CARCINOGENICITY** | Y[16] | Y[17] |
| **MUTAGENICITY** | | |
| *In Vitro* | Y}[18] | Y} [19] |
| *In Vivo* | Y} | Y} |
| **ENVIRONMENTAL** | | |
| Bioaccumulation | Y} | N |
| Bioconcentration | Y}[20] | N |
| Oct/water Part. Coeff. | Y} | N |
| Acute Fish | N | N |
| Acute Daphnia | N | N |
| Subchronic Fish | N | N |
| Subchronic Daphnia | N | N |
| Chronic Fish | N | N |
| **AVIAN** | | |
| Acute | N | N |
| Reproductive | N | N |
| Reprodcutive | N | N |

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[15] Guide at pp-23; 33-34.

[16] 43 Fed Reg at 11112
"Cancer" listed

[17] Guide at pp-21.

[18] 43 Fed Reg at 11112; 11115 at Comment 15
"Mutagenicity" listed/ *in vivo* vs *invitro* discussed; discussion of "Ames test".

[19] Guide at pp-23.

[20] 43 Fed Reg at 11112; 11115 at Comment 16.

(9)

CAS: 124-73-2; 75-61-6; 353-59-3
Chem: 1,2-dibromotetrafluoroethane; dibromodifluoromentahne; bromochlorodifluoromethane
Title: On the Acute toxicity of Halons
Date: 7/2/7o
Summary of effects: tremors, motor paralysis

# 2429

FROM THE RESEARCH LABORATORIES OF KALI-CHEMIE AG

# ON THE ACUTE TOXICITY OF HALONS

by

K W von Eicksted, H W Paucksch and W Höppe
with technical assistance from R Braeckow and H Hahne

## SUMMARY

The toxic concentrations of Halons 1202 ($CF_2Br_2$), 1211 ($CF_2ClBr$) and 2402 ($CF_2BrCF_2Br$) were studied experimentally in animals using an airtight Plexiglass cage through which the test Halon/air mixture was passed. The concentration in the mixture of each of the Halons studied was steadily raised. Control of the Halon concentrations in the air mixtures was achieved by means of floating-body gauges. The Halon concentrations were continuously recorded by gas density monitors.

In order to determine the toxic concentrations of the three different Halons the onset of toxic symptoms was established by observation of rats. The symptoms established in the rats were compared as regards dosage dependence by reference to the Halon concentration recorded.

Toxic symptoms such as tremor, narcotic motor paralysis, cramps and respiratory disorders were produced by concentrations in air of greater than 6 vol % Halon 1211 (more than 99 vol % pure). Mixing Halon 1202 with 1211 increased the toxicity of Halon 1211.

The toxic symptoms caused by inhalation of pure Halon 1202 in air (purity 99.9 vol %) were produced by concentrations less than 2 vol %.

The toxic concentration for observable toxic symptoms due to Halon 2402 inhalation was found to be between 1.2 and 3.2 vol % in air.

By experimentation at higher Halon concentrations the mean lethal doses were calculated in vol % from the number of rats dead. The lowest LD50 acute toxicity was that for Halon 1211 of fire-extinguisher purity grade 99.6%. Its LD50 was 22.5 vol %, while the corresponding values for Halons 2402 and 1202 were 5.3 and 4.0 vol % respectively for the pure compounds in air.

Experiments on single cats showed, as had been found for the rats, that the Halon 1211 concentrations which would cause toxic symptoms were higher than for Halon 2402.

## Introduction

The properties and applications of the traditional fire-extinguishing agents water, powder and $CO_2$ have long been known. The development of the technique has brought new risks and has defined the limits of their applicability more sharply. Efforts were therefore made to tackle fires, especially developing fires, in other ways. For this purpose compounds which influence the combustion process chemically were suitable.

The organohalogens (1,2) were found to be specific reactive agents. The simplest compound of this type was carbon tetrachloride. Experience obtained with this soon led to limitation and finally to complete prohibition of its use as an extinguisher in many countries. A summary has been published (3) of accidents with carbon tetrachloride in the USA. Its use as an extinguisher has been forbidden in the German Federal Republic since 1964 (4). Simple brominated hydrocarbons such as methyl bromide were found to be unsuitable because of the toxicity of the pure substance (5).

The successor to carbon tetrachloride, chlorobromomethane (CB), was at once found not to be harmless, so we may understand why the whole halogeno-hydrocarbon group found only limited application in fire extinguishing. For the same reason the maximum allowed amount in W. Germany was limited to 2 litres per extinguisher (22,23). A fundamental change began with the increasing use of fluorinated hydrocarbons. Research on the relation between their chemical structure and their toxic action had already been carried out (8,9).

The difficulty experienced in rendering compounds containing several halogens in one molecule comprehensible to non-chemists very soon led to a simplified description of these extinguishing materials (10).

The normal English-language generic term "halogenated hydrocarbon" was contracted to "Halon". To this is added a number, normally four-figured; the left-handmost digit indicates the number of carbon atoms in the molecule, then comes the number of fluorine, then chlorine then (right-handmost) bromine atoms. Terminal zeros are omitted. If one of these elements is not present, a zero is written in its place.

Of the many theoretically possible fluorinated Halons only a few have been of considerable significance. They are as follows:

| | | |
|---|---|---|
| Halon 1202 | Dibromodifluoromethane | $CF_2Br_2$ |
| Halon 1211 | Bromochlorodifluoromethane | $CF_2ClBr$ |
| Halon 1301 | Bromotrifluoromethane | $CF_3Br$ |
| Halon 2402 | 1,2-dibromotetrafluoroethane | $CF_2BrCF_2Br$ |

Their physical and chemical properties, methods of use in fire-extinguishing and toxic effects have already been studied and reported (6,7). The authors concluded that of all the compounds studied Halon 1211 possesses the best combination of properties, activity and tolerability. Thereafter developments occurred differently in the USA and Europe. While Halon 1301 was introduced in the USA (11), Halon 1211 was preferred in Europe (12).

Most recently Halon 2402 has also been more strongly recommended than Halon 1211 (13,14,15). Since the literature contained very little on the subject of Halons 2402 and 1202 and their action in the undecomposed state on experimental animals (7), it was decided to compare these substances with Halon 1211.

A comparison of Halons 1211 and 2402 seemed even more necessary, since both were entered in the "Underwriters Classification 5", i.e. in the same group as carbon dioxide, propane and fluorotrichloromethane, so that differences in toxicity were not recognised.

Use of hand extinguishers against a fire always involves the use of only a limited quantity of Halon. For this reason Halons have been used for some years for stationary installations, automatic fire

protection of rooms and so on (12,16,17), always in such a way that people are only briefly exposed to the extinguishing substance. In both cases the risks involved in using the conventional extinguishers, i.e. $CO_2$ are well known (18,19). Likewise the safety recommendations are also well understood (20,21).

## Statement of the problem

Our purpose was to establish the acute toxic activities, on brief exposure to inhalation, of those fluorine-, chlorine- and bromine-containing compounds which seemed in the light of their previously discovered properties to be especially suitable for use in fire extinguishing. We required to compare the concentrations in air at which the compounds produced toxic effects in animal experiments.

## Properties of the Halons

The Halons used as fire-extinguishing compounds, i.e. 1211, 1202 and 2402, have in some respects very different properties, some of which are shown in Table 1.

TABLE 1

| Halon |
|---|
| Formula |
| Mol wt |
| M Pt (°C) |
| B Pt (°C) |
| Max allowed Conc (Vol - ppm) |
| Underwriters Classification |

## Purities of the Halons used

The experiments were carried out with Halons of varying purity grades so as also to observe the effect of the impurities on the animals' behaviour. Table 2 shows the composition of the materials used.

Product 1 was a specially purified Halon 1211

Product 2 was Halon 1211 of normal commercial quality

Products 3 & 4 were obtained by mixing product 2 with pure Halon 1202
Product 5 was a specially purified Halon 1202
Product 6 was Halon 2402 of normal commercial quality
Product 7 was the raw product from which product 6 was obtained.

TABLE 2

Composition of the Products Used (1-7) in Vol %

| Compound Description / Formula | |
|---|---|
| Various | |
| Impurities | |

## Analysis

The composition of the Halons were determined by gas chromatography. The values given in Table 2 for products 1, 2, 5, 6 and 7 are the liquid compositions, and no significant changes in composition were likely on vapourisation. For products 3 and 4 the values tabulated were determined in the gas-phase in the mixture dosed.

## Organisation of experiments

1. Physical chemical methods

In view of the differing boiling points two different methods of dosing were adopted.

(a) Halon 1211 was taken from a steel vessel and fed in using a floating-body gauge and needle valve. The necessary heat for vapourisation was provided externally by immersion in water thermostated to 35°C. The Halon 1211 flow was mixed in a T-piece with the amount of air necessary to produce the required concentration. The Halon concentration was varied by varying the amount of Halon fed, keeping the air-flow rate constant at 50 Nl/min during the experiment.

(b) In dosing Halons 1202 and 2402 another method had to be used in order to prevent condensation of the materials before dilution. These substances were evaporated from a thermostated vessel by a small measured air-flow, then at once mixed with the main air-flow in a T-piece. Variation of the Halon concentration was effected by varying the amount of evaporated Halon/air mixture fed.

Measurement of mixture densities was effected using two Pollux recording gas and densitometers (limits of error ± 1% of scale-end value). The scale ranges of measurement were

1.20 - 1.90 gm/cm$^3$
and 1.20 - 2.95 gm/cm$^3$ respectively

In addition to the recording, the gas density was read and noted at one minute intervals.

Halon concentrations in the air stream were determined using gas densitometers that were connected either in parallel or beyond the experimental enclosure. Where the parallel arrangement was used the gas flows were divided in proportion to the volumes of the densitometer and the experimental enclosure so that we could at any time know the gas density and hence the concentration in the enclosure. In the second arrangement the whole exhaust flow from the experimental enclosure was passed through the densitometer, which therefore registered the enclosure concentration approx 30 secs previously. This slight disadvantage was compensated by the simpler experimental array needed.

Fig. 1 shows the experimental arrangement 1 used for Halon 1211, with gas densitometer set up in parallel, while experimental arrangement 2 is the version used for Halons 1202 and 2402, with gas densitometer connected at the exhaust side of the enclosure.

2. Animal experiment methods

Male Sprague-Dawley rats of the Ivanova strain (Kisslegg/Allgäu) of body weight 160-180 g, fed ad libitum on (?) standard food and

dechlorinated tapwater, were used in the first experimental arrangement. Until the start of the experiment the animals were kept in macrolon cages at a constant temperature of 21 ± 1°C, air humidity 55 ± 10% water, on granulated wood shavings, and were subjected to a 12-hour light-dark cycle. They were obtained from the breeding unit in an infection-free state and acclimatised under controlled conditions at the Kali-Chemie AG animal house for several weeks before the experiment.

10 rats were used for each experiment on the Halons. The animals were placed in the plexiglass experimental enclosure (floor area 50 x 70 cm), in which they could move about freely on a blotting paper floor. This enclosure, in which the animals could easily be observed, was airtight. Initially the normal behaviour of each animal group in a current of pure air was observed. Only after this time, which could be called the exploration phase, and lasted at least 10 minutes, after which the animals' behaviour no longer varied significantly, was the Halon/air mixture exposure started, and its effect on the animals established by observing the onset of toxic symptoms.

After determining the concentration which would produce toxic symptoms, we then determined for each gas mixture the concentration which killed half the experimental animals. For this a gradual increase in the Halon concentration was applied, as is shown separately for each experiment in Figs. 1 - 8. Calculation of the Halon concentration lethal to half the experimental animals was carried out in accordance with the method of Litchfield and Wilcoxon by determining the mean lethal dose (n = 10) for each of the Halon concentrations measured in the lethal range. The lethal concentrations were expressed in Halon volume per cent. The calculation of the mean lethal dose was thus given by the Halon concentration, expressed as vol % in the inhaled air mixture (shown as LD in Figs. 2 and 4 - 7). The particular doses used as a basis for this calculation resulted from observation of the Halon concentration up to the point where one or several animals died acutely.

After the end of the experiment, at which point clean air was passed into the experimental enclosure, the surviving animals were

returned to the macrolon cage previously described, and were observed periodically over the next 24 hours. No further deaths were observed during this period, if the animals had recovered during the first 2-4 hours after the end of the experiment.

In the second series of experiments 6 adult cats were used in order to allow more precise observation of the behavioural changes in a particular animal. The same experimental arrangement was used for introduction of the gas mixture as in the rat experiments.

## Results

1. Observations in rats

(a) Action of Product 1. On exposure to increasing concentrations of 99.9% Halon 1211 (Product No. 1) a reaction was already noted in the rats during the first 10 minutes (after the end of the exploration period) of the experiment. All 10 animals were seen to be uneasy, and shook their heads repeatedly. As can be seen from Fig. 1, the Halon 1211 concentration in the inhaled air had not yet increased to 3 vol % during this time. In the next 5 minutes the animals also displayed an increased grooming drive. 20 - 30 minutes after the start of the grooming drive weakened somewhat, and the stereotyped head-shaking movements, which were accompanied by eye-blinking, ceased.

[FIGURE 1]

30 - 40 minutes after the start the stereotype behaviour increased, and was accompanied by gentle shaking of the raised fore-paws. The Halon 1211 concentration now reached 3 vol %. Above 3 vol % some of the animals began to look for a way out of the enclosure. 60 - 80 minutes from the start, at a Halon concentration of 4 vol % (see Fig.) the rats' behaviour had not yet changed significantly. The animals' unease decreased again somewhat up to the hundredth minute. No further

significant change in behaviour was seen below 6.5 vol % Halon. Only above 7 vol %, reached after more than 2½ hours, were the first symptoms of a pathological nature observed; these consisted of motor disturbances, occurring periodically in a few animals. Temporary jerky movements of the extremities and giddiness while moving were also noted. After 3 hours, at 7.9 vol % Halon, the animals began to tremble, became slightly cyanotic and their breathing rate increased more. As the concentration rose further the tremors became more severe and were replaced by jerking (very short-duration cramps). The latter symptoms occurred at intervals in some of the animals and when the Halon concentration reached 9 vol % two of the 10 rats lay on their stomachs and had attacks of clonic-tonic convulsions. At 9.7 vol % seven of the 10 rats were on their stomachs and subject to these attacks. These animals displayed pronounced cyanosis. Strong tremor and increased breathing rate were observed in the intervals between the generalised convulsions. At 11 vol % all the rats were lying on their stomachs, with bouts of severe clonic-tonic convulsions. As before marked tremor and very frequent and forced breathing were noted in the intervals between attacks. After the rats had breathed Halon 1211 at 11 vol % in air for 20 minutes, experiment 1 was terminated by flushing with fresh air. Fifteen minutes after the beginning of fresh air flow all the rats were again moving normally except for a slight atactic gait in some animals.

(b) Action of Product 2. In the second experiment Halon 1211 was again used, this time of 99.6% purity. The Halon concentration in the experimental enclosure was increased more rapidly than in the previous experiment, as can be seen from Fig. 2.

[FIGURE 2]

During the first 20 minutes, during which in contrast to experiment 1 the Halon concentration increased to over 5 vol % (see Fig. 2), no differences could be discerned in the behaviour of the 10 rats used in this experiment compared with that seen

during the same period in the first experiment. At a concentration of 6.1 vol % of product No. 2 one of the 10 animals developed clonic convulsions, briefly preceded by slight tremor. At 7.3 vol % several animals displayed slight tremor and accelerated forced breathing. Cyanosis of the skin now began in all the animals. Only one of them had periodic clonic convulsions, but without lying on its stomach or side. Between convulsions it moved normally. At 8-9 vol % half the animals were lying on their stomachs, and the rest walked very unsteadily (staggering) and displayed severe tremor. Several animals splayed out their rear extremities. At 10 vol % 8 animals were on their stomachs or their sides, but only 2 had clonic convulsions. On further increasing the Halon concentration, we observed most of the rats to be in a narcosis-like state with motor paralysis, and increased cyanosis. This cyanosis together with the strong tremor during clonic convulsion, and breathing disorders, could clearly be observed at 13.5 vol % Halon concentration. Further increases in concentration induced a more and more narcosis-like state in the animals, interrupted by strong tremor and occasional convulsions. Up to 20 vol % Halon the symptoms remained as described, with intensification of cyanosis and respiratory disturbances.

The first two animals died when the Halon 1211 (Product No. 2) concentration reached 21.4 vol %. The Halon 1211 concentration was further increased to 22.7 vol %, at which level 6 of the 10 animals had died, before the experiment was ended by passing in clean air. One more animal died during the replacement of the Halon/air mixture by clean air. One hour after the end of the experiment the surviving rats had recovered to such an extent that they were able to move about easily, still with slight ataxia.

A repeat experiment on 10 rats with product No. 2 involved about the same rate of Halon concentration increase as the previous one, and the same symptoms were seen at comparable gas concentrations, so that we may omit a detailed account of the experimental conditions. Once again the mean lethal

concentration for product 2 lay between 22 and 23 vol %. The Halon 1211 described as product No. 2 had therefore a mean lethal dosage of 22.5 vol %.

(c) Action of Product 3. In a fourth experiment, Halon 1211 of 92.7% purity, described as product No. 3, was studied. As we have previously stated this sample of Halon 1211 contained 7.0 vol % Halon 1202. As in experiment 1 the Halon concentration in the experimental enclosure was raised slowly : the Halon concentration at various times are shown graphically in Fig. 3.

[FIGURE 3]

Note. Caption says "Product No. 2"
I think it should say "Product No. 3".

Once again there was no detectable difference in the first 20 minutes between the behaviour of the 10 rats in this experiment and of those in the first experiment over the same period. 20 - 40 minutes after the start, during which time the Halon concentration passed 3 vol %, a narrowing of the animals' eyes was observable. After 75 - 80 minutes, at 4.5 vol % Halon, incipient cyanosis of the visible skin areas was first noted. At 100 - 120 minutes, Halon level 5.3 vol %, increased breathing rate was noted, in addition to the more pronounced breathing movements seen with increasing Halon concentration. Several animals became subject to intermittent tremor when the Halon concentration reached 6.3 - 6.4 vol %. About 140 minutes after the start one animal had a clonic-tonic convulsion lasting less than a minute. Slight nasal secretion began as the Halon level passed 7.0 vol %, and two more animals now displayed transient clonic-tonic convulsions. After more than three hours, as the Halon level passed 8.5%, one rat lay on its side, and had brief clonic-tonic convulsions. Above 9 vol % 6 of the 10 rats were lying on their stomachs or their sides in a narcosis-like state, with superimposed tremor and transient convulsive attacks. Cyanosis increased and was very pronounced at a Halon concentration of 11 vol %. When

the 10 vol % Halon level was reached all the animals were on their stomachs or their sides, and subject to periodical clonic-tonic convulsions.

After 5 hours the experiment was ended at the 11 vol % Halon level, by passage of clean air. 12 minutes after the end of the experiment all the animals were moving, but showed signs of slight ataxia, which could still be observed in some of them 40 minutes after ending the experiment.

In a 5th experiment product No. 3 was again studied on 10 rats, but the rate of concentration increase was more rapid. The levels reached at various times are shown graphically in Fig. 4.

[FIGURE 4]

During the first 20 minutes the behaviour of the animals was the same as in the previous experiment. After 30 minutes at a Halon concentration of about 4.5 vol %, an increase in the breathing rate was noted. Once again a narrowing of the rats' eyes was also seen. At about 6.5 vol % tremor set in together with some locomotor co-ordination disturbance and incipient cyanosis. In this experiment the first rat suffered clonic-tonic convulsions at a Halon concentration of 6.85 vol %. The stomach or side-lying position was observed at approx. 8 vol %. As the Halon concentration rose the cyanosis, tremor, the number and duration of the convulsive episodes and the frequency and difficulty of breathing increased, and the rats went more deeply into the narcosis-like state. At 10 vol % all of them were lying on their sides or their stomachs.

At a concentration of 18.3 vol % product No. 3 the first rat died, at 20.4 vol % four of them, and at 21% five of them were dead. Experiment 5 was ended at a Halon concentration of 21%. One rat died a few minutes after passage of fresh air was started. The remaining animals recovered about as fast as those in the previous experiment, but remained somewhat atactic for several hours.

(d) Action of Product 4. In a sixth experiment the Halon 1211 sample described as product No. 4 was tested: it was 79.9% pure, and contained 20.0 vol % added Halon 1202. The rate of increase of Halon concentration in the enclosure is shown graphically in Fig. 5.

[FIGURE 5]

During the first 20 minutes of the experiment (in which 10 rats were again used) as before no behavioural difference from earlier experiments was observable. After 20 minutes, at a Halon level of 3.6 vol %, an increase in breathing rate was noted. Narrowing of the eyes was also observed in this experiment. Cyanosis and the onset of tremor occurred in several animals after 30 minutes, as the Halon level passed 6 vol %. The animals' breathing was more rapid and more strained. After 40 minutes cyanosis and tremor had considerably increased in all the animals. 45 minutes after the start, when the Halon concentration reached 7.7 vol %, motor disturbances were seen in three animals, who developed a staggering gait, while six animals passed into a narcosis-like state. One further animal had a brief clonic-tonic convulsive episode. Further increasing the Halon level to 10 vol % intensified these symptoms and the narcotic state. The first animal died at 14.0 vol %, two had died at 16.4 vol %, four at 17.5 vol % and six at 18.8 vol %.

After 2½ hours the experiment was ended (at 18.8 vol % Halon) in the same way as in the previous experiments. For several hours more the rats showed slight cyanosis and ataxia.

(e) Action of Product 5. In a seventh experiment the Halon sample described as product No. 5 was investigated using 10 more rats. This sample contained 99.9 vol % Halon 1202. The increase of the Halon concentration in the enclosure during the experiment is shown graphically in Fig. 6.

[FIGURE 6]

Only 5 - 10 minutes after the start of this experimen. at a Halon level of approx 0.4 vol % slight motor disturbances, namely staggering gait, were observed. The other known symptoms, unease, blinking and stereotypies were also observed. At 0.9 vol % Halon the motor disturbances increased significantly. 40 minutes after the start, at 1.1 vol %, several animals began to breathe more rapidly. At 1.5 vol %, 50 minutes, tremor set in in several rats, and one animal had a brief clonic-tonic convulsion. At this Halon level all the animals showed more rapid, forced breathing and cyanosis of the visible skin areas. 65 minutes after the start at 1.7 vol % Halon four of the animals were lying on their stomachs and suffered periodical clonic-tonic convulsive attacks. The symptoms increased greatly up to 2.2 vol % Halon, and copious flow of saliva began. The convulsive episodes became continuous clonic-tonic convulsion of mild to moderate intensity. Over 3 vol % all the animals were in a narcosis-like state lying on their stomachs or side, and most of them were in permanent convulsions.

At a Halon concentration of 3.0 vol % the first animal died. At 3.8 vol % two, at 3.9 vol % four, and at 4.0 vol % eight of the 10 animals had died.

At a Halon concentration of 4.1 vol % the experiment was ended in the usual way. 30 minutes later the surviving two rats were still lying on their stomachs, with strained breathing and cyanosis. Sedation could still be seen in both of them for several hours.

(f) Action of Product 6

In an eighth experiment product No. 6, Halon 2402, was investigated using a further 10 rats. The purity of this Halon sample was 99.4 vol %. The increase of Halon concentration in the enclosure during this experiment is shown in Fig. 7.

[FIGURE 7]

During the first 5 minutes of the experiment stereotypies and unease were again observed, as in the previous experiments. Marked motor co-ordination disturbance set in at 1.2 vol % Halon. The animals staggered backwards and forwards, stood on their splayed hind legs in a defensive position and exhibited pronounced tremor of the extremities. The breathing rate was considerably accelerated. Between 10 and 20 minutes after the start sedation and rapidly increasing cyanosis began. At 2.5 vol % Halon 2402 this sedation became a narcosis-like state in 3 of the animals, which lay on their sides. At 2.8 vol % clonic convulsions began in 4 rats, which were lying on their sides. The other animals staggered backwards and forwards, falling on their sides and getting up again. The tremor was now very marked. When a Halon level of 3.5 vol % was reached all the animals were lying on their stomachs or their sides and had clonic convulsions.

As the Halon concentration increased further 2 of the 10 rats died at 5.7 vol % Halon 2402, and 2 more at 5.8 vol %.

89 minutes from the start this experiment was ended in the usual way. The Halon concentration at this point was 5.8 vol %. Four minutes after the end of the experiment 2 more rats died, so that 6 of the 10 did not survive the experiment. Two hours later the surviving animals were behaving normally, apart from slight sedation.

(g) Action of Product 7

In the ninth experiment Halon 2402 of 96.5% purity, described as product No. 7 was studied in 10 rats. The measured Halon concentrations for this experiment are shown graphically in Fig. 8.

[FIGURE 8]

During the first 5 minutes of this experiment the behaviour of the animals did not differ significantly from that seen in the same part of the previous experiment. In the next 5 minutes disturbance of the animals' motor co-ordination was noted: they

staggered, fell repeatedly on to their sides and got up again. Fifteen minutes after the start the animals' motor activity decreased. Twenty minutes after the start, at 2.3 vol % Halon, cyanosis set in, the breathing rate increased significantly, and some of the animals were transiently lying on their stomachs or their sides, and displaying marked tremor. At 3.2 vol % Halon first one rat suffered a clonic convulsive episode, while lying on its side, and a few minutes later 7 of the rats had mild continuous clonic convulsions. The remaining animals lay on their stomachs or sides. As the Halon concentration rose the cyanosis and respiratory disturbances increased. These symptoms had been observed in all the animals (which were in a narcotic state) by 80 minutes from the start (Halon concentration 4.6 vol %).

The first animals died when the Halon level exceeded 5.5 vol %. At 5.6 vol % 3 had died, and at 5.7 vol % 5 more died. 138 minutes after the start the experiment was ended in the usual way. The 2 surviving animals still showed signs of slight sedation 2 hours after the end of the experiment.

2. Comparison of the active concentrations in rats for the various Halons

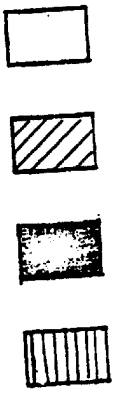
The above results showed that the toxic concentrations of the different Halons vary considerably. In order to compare the lowest concentrations at which the individual Halons showed activity, it seemed advisable to set out the individual symptoms which we regarded as toxic.

From the rising concentration experiments, the first symptom caused by products 1 (99.9% Halon 1211), 3 (Halon 1211 + 7% Halon 1202), 4 (Halon 1211 + 20% Halon 1202), 5 (99.9% Halon 1202) and 6 (99.4% Halon 2402) was respiratory disturbance. With product 6 tremor began at the same time as respiratory disturbane, while product 7 (96.5% Halon 2402) caused tremor, respiratory disturbance, and the paralysis or muscular relaxation described as a narcotic effect all at the same concentration.

Fig. 9 shows these toxic activities for the various Halons and Halon mixtures, as found in the above experiments, presented graphically with the vol % concentrations at which they began.

FIGURE 9

Toxic Symptoms in Rats, Males, 160-80 g



Tremor

Respiratory disturbance

Paralysis

Convulsive threshold

Comparison of the toxic concentrations in this figure shows that Halon 1211 is tolerable in higher concentrations than the other Halons, before the toxic activity appears, in this case solely as nervous system effects, such as convulsions and the narcosis-like state we described as paralysis, during which the rats lay on their stomachs or their sides as we have already described.

The narcosis-like state we described as paralysis appeared last with products 2 and 3, and clearly demonstrated a dependence on the percentage of contaminant in the Halon 1211. Such a dependence can also be seen when the lethal concentrations are compared, as in Fig. 10, where these are presented graphically.

From the mean lethal doses (LD50) shown in Fig. 10 we established that there was no statistically significant difference between the LD50s for product 2 (22.5 vol %) and product 3 (20.9 vol %). The differences in the toxicity of the various Halons are even more apparent from the lethal concentrations (Fig. 10) than from the minimum levels causing neurotoxic symptoms such as tremor or convulsions (Fig. 9).

FIGURE 10

Acute LD50 in rats (Male 160-180 g) with upper and lower limits of confidence.

3. Results of experiments in cats

In a study of Halons 1211 and 2402 in cats we used products 2, 6 and 7, taking 2 cats in each case, one at a time. So as to prevent them moving about in the cage, which would have complicated detailed observation, we placed soft stuffed plastic objects in the experimental enclosure. The cats could still sit and lie down without hindrance. All the animals were accustomed to passage of air through the enclosure before the Halon experiment was begun.

(a) Activity of Product 2

In the first of the 6 experiments no toxic symptoms were observed in the first 15 minutes, during which the Halon 1211 (product No. 2) level rose to 1.5 vol %. After 16 minutes, at 1.8 vol %, the cat periodically shook its head. After 25 minutes, at 2.7 vol %, the cat became uneasy and looked for a way out. At 3.0 vol % it made slight defensive movements with one of its fore-paws. After 33 minutes, at 3.5 vol %, the cat took up a lowering position, and began chewing and licking movements. After 42 minutes it again became uneasy, pressed itself backwards with slightly jerky movements, and showed significant pupil dilatation. The Halon concentration was then 4.1 vol %. After 45 minutes, at 4.4 vol %, the cat was making jerky head movements and defensive movements with its forepaws, and had considerably dilated pupils. Three minutes later at 4.6 vol % slight saliva flow and ataxia was observed.

At 4.8 vol %, 50 minutes from the start, the same symptoms were observed, and at 5.1 vol %, 52½ minutes clonic tonic convulsions began. After 53 minutes the experiment was terminated in the usual way. Two minutes later the cat was still breathing harshly but was otherwise normal.

In the next experiment (No. 2) no significant behavioural change was seen for the first 40 minutes, during which time the Halon concentration reached 3 vol %. When it reached 3.1 vol %, after 45 minutes, the cat began to be uneasy, shook its head occasionally and swallowed and licked itself repeatedly. After 55 minutes, at 3.7 vol %, the animal was looking for a way out, moving unsteadily; it was uneasy and shook its head from time to time. After 70 minutes, at 4.9 vol %, dilated pupils, slightly jerky defensive movements and ataxia were observed. After 72 minutes, at 3.5 vol %, clonic convulsions set it, which occurred at intervals as the concentration rose over the next 2 minutes to 5.9 vol %.

74 minutes after the start the experiment was terminated in the usual way. Less than 1 minute after introduction of fresh air the convulsions ceased, and over a few minutes the behaviour of this cat became normal. Like the first one, this cat was still shy and frightened the following day.

(b) Action of Product 6

In the third experiment Halon 2402 of 99.4 vol % purity (product No. 6) was studied. Five minutes after the start, at a Halon level of 0.3 vol % the cat had somewhat enlarged pupils and was blinking its eyelids. After 10 minutes, at 0.5 vol %, head shaking, slight tremor, unease and atactic gait were observed. After 30 minutes, at 1.3 vol %, the symptoms were about the same as after 10 minutes. At 40 minutes, 1.8 vol %, the animal's unease disappeared, and it lay on its stomach, the ataxia being now more pronounced. At 47 minutes, 2.2 vol %, tonic convulsions began, the animal lying on its side. On further increasing the Halon concentration to 2.6 vol %, the convulsions became clonic tonic and the animal rolled onto its stomach. Two and half minutes after the end of the experiment the animal had greatly recovered apart from repeated head-shaking.

Product No. 6 was again studied in the fourth experiment. In the first 5 minutes the cat's behaviour was the same at the

same Halon levels as in experiment 3. After 10 minutes, at 0.5 vol %, unease and head-shaking were observed. After 16 minutes, at 0.9 vol %, a slightly atactic gait was seen. At 20 minutes, 1.1 vol %, the cat was very atactic and gasping for breath. At 30 minutes, 1.4 vol %, there was slight body tremor, marked unrest and ataxia with gasping breathing. At 40 minutes, 1.8 vol % marked tremor and ataxia and pronounced gasping were observed. At 50 minutes, 2.4 vol %, the symptoms were much the same as after 40 minutes. At 54 minutes, 2.5 vol %, the animal lay on its stomach, then rolled onto its side, with clonic-tonic convulsions.

After termination of the experiment the cat at first remained on its side, then stood up after 7 minutes, and recovered rapidly apart from slight ataxia of rather longer duration.

(c) Action of Product 7

In a fifth experiment 96.5 vol % Halon 2402 (product No. 7) was studied. Four minutes after the start, at 0.2 vol % Halon, the third (?) cat showed slight signs of unease. At 10 minutes, 0.5 vol %, more marked unrest was noted, together with slightly atactic movements, occasional head-shaking and blinking. At 15 minutes, 0.8 vol %, there was increased ataxia erection of the fur and marked unrest. At 30 minutes, 1.4 vol %, the animal lay on its side after displaying more pronounced ataxia. At 35 minutes, 1.8 vol %, we also noted an optisthotonic fixed head position. At 40 minutes, 2.1 vol %, in addition to the optisthotonus, the animal was lying on its side, its eyes closed and breathing in gasps. 44 minutes after the start, at a Halon level of 2.2 vol %, clonic-tonic convulsions set in. After 47 minutes altogether, a concentration of 2.3 vol % was reached, and the convulsions became continuous. Two minutes later the experiment was terminated in the usual way. Six minutes after termination the cat was sufficiently recovered to move about, albeit atactically. After about one hour it had completely recovered.

In experiment 6, product No. 7 was again tested. This time the cat arched its back and was shaking its head in the first minutes of the experiment, at a Halon level of 0.2 vol %. At 10 minutes, 0.5 vol %, it was blinking and repeatedly shaking its head. At 15 minutes, 0.8 vol %, its fur stood erect as well. At 20 minutes, 1.1 vol %, it was uneasy, moved atactically and jerkily and its fur was still erect. At 30 minutes, 1.4 vol % it showed the same symptoms, with marked ataxia and unease. At 40 minutes, 1.9 vol %, saliva flow began and the marked ataxia was replaced by a lying posture, first on its stomach then on its side.

The saliva flow increased, the animal got up again, with very atactic movements, and then again lay down, at 48 minutes, 2.4 vol %. After 57 minutes, at 2.7 vol % Halon, clonic-tonic convulsions set in, the animal lying on its side. After termination of the experiment 10 minutes passed before the animal got up spontaneously, and it then recovered rapidly.

(d) Summary of the activity in cats

Summarising the activity in cats during these 6 experiments we see that behavioural changes such as unease and stereotyped behaviour first occur above 1.5 vol % with Halon 1211 (product No. 2), while the same changes are seen at 0.5 vol % when Halon 2402 is studied (products 6 and 7).

In both experiments with Halon 1211 we could not before convulsions began detect any narcosis-like state similar to that observed with Halon 2402. The concentrations at which the onset of convulsions occurred are presented graphically in Fig. 11.

[FIGURE 11]

Convulsion thresholds in male and female cats

Although the convulsion thresholds are different, the cat experiments also show that the toxic concentrations of Halon 1211 (product No. 2) are sufficiently higher than those for

Halon 2402, either as product No. 6 or No. 7, so that Halon 1211 may be considered less toxic.

## Discussion

The comparison of Halons 1202, 1211 and 2402 was of especial interest, since these three compounds are well known as fire-extinguishing agents. The difference in the lethal concentrations of Halon 1211 and of the other two Halons seemed remarkable.

If one compares the Halon 1211 and 2402 concentrations quoted by Engibous and Torkelson (7) as being just not lethal in rats, here too one can see a significant difference between the two fire-extinguishing agents. The authors report that exposure for 1 hour to Halon 1211 concentration between 150,000 and 200,000 ppm was not quite lethal, while the comparable values for Halons 2402 and 1202 were 60,000 and 40,000 ppm respectively.

These results give concentrations which are just tolerated by the rats, and compare well with the experimental results obtained in our work, if when speaking of the tolerability of a compound one restricts oneself to its lethal activity, as this is most accurately assessed in animal experiments.

The authors referred to above, also give the lethal concentrations in rats for Halon 1211 at various exposure durations. Comparison of the mean lethal dose given in the present work for normal commercial Halon 1211 (product No. 2) with the values quoted by these authors, shows a good agreement provided allowance is made for the fact that in our experiments the Halon level was raised steadily, while the data given by Engibous and Torkelson related to continuous exposure to a constant concentration sufficient to cause death.

A further comparison of lethal concentration values for the extinguishing agents used here may be found by referring to the work of Gross (6).

The presence of added Halon 1202, which is quite toxic, in Halon 1211 rendered the Halon 1211 itself more toxic as might have been expected. When the relation between the mean lethal dose and Halon 1202 percentage in Halon 1211 is calculated, the resulting increased toxicity of Halon 1211 is obtained, and is presented graphically in Fig. 12.

[FIGURE 12]

LD50 in vol % for Halon 1211/1202 Mixtures in Rats

Concerning this increase in Halon 1211 toxicity on admixture of Halon 1202 it should be remembered that there was no significant difference between the toxicity of 99.6% Halon 1211 and 92.7% Halon 1211 (containing 7 vol % Halon 1202). When small amounts of Halon 1202 are present in Halon 1211, for example the 7 vol % contained in product No. 3, it must be impossible to observe the difference in tolerability with any experimental arrangement of the type we used.

During all the experiments described here the Halon concentration was gradually increased, so as to allow observation of the animals' reaction at the different concentrations. Using this method, with continual increase of Halon concentration in the experimental enclosure it was possible to distinguish between symptoms typical of animals' reactions to a strange gas and those due to its actual toxicity. For example we did not consider that the animals' unease, sniffing around and head-shaking were pathological in nature, while the cyanosis, not seen in all experiments, should be so considered. With pure Halon 1211 it first occurred over 7 vol %, while Halon 1202 (product No. 5) already caused it at 1.5 vol % and with Halon 2402 the corresponding value was of the order of 2 vol %. In considering the experiments described here we should assess these toxic effects in relation to the experimental method used, since the concentrations producing them were reached at different points in time. For this reason the experiments were repeated even with the less toxic products so as to allow a second observation of the toxic symptoms produced using a more rapid gas level increase.

It can be seen that the rate of increase of Halon concentration must have an effect on the onset of toxic symptoms, from the results concerning

the onset of convulsions in rats which inhaled product No. 4 (Halon 1211 and 20% Halon 1202). In experiment 6 the concentration of Halon 1211 which contained 20% Halon 1202 and so was more toxic was raised more rapidly than in experiment 4, in which the concentration of the purer less toxic product No. 3 (see Fig. 10) was raised more slowly.

For the pure forms of Halons 1202, 1211 and 2402 we used experimental conditions involving slow increase in the gas concentration (see Figs. 1, 3, 6 and 8), so that we were able to compare not only the lethal effects caused by rapid increase in concentration, but also the toxic symptoms caused by low concentrations.

The experiments with cats should have confirmed the differences between Halons 1211 and 2402 found in rats. Changes in behaviour during a single experiment could be observed more easily in the cats than the rats. Comparative experiments with ammonia showed that even at 0.05 vol % $NH_3$ cats were already uneasy, drooled and had dilated pupils. Head-shaking, licking and sneezing were also seen at this $NH_3$ concentration.

Taking into account the observations on the obviously behaviourally more sensitive cats we conclude that as well as cyanosis the other toxic symptoms shown in Fig. 9 most readily allow a comparison of the Halons studied.

In comparing the toxic symptoms and the lethal doses we conclude that the maximal Halon 1202 toxicity given by the authors cited above is derived not only from the lethal activity, but also from the reversible toxic actions seen at lower concentrations. (See Fig. 9). The same is true for the difference described between Halons 2402 and 1211, however in this case because of the difference between our experimental conditions and those chosen by the other researchers, the possibility cannot be excluded that in respect of the reversible toxic symptoms the difference between pure Halon 1211 (product No. 2) and Halon 2402 may in fact be even greater than might be supposed from the lethal doses quoted in the literature.

At any rate narcotic effects from Halon 1211 are only to be expected at concentrations significantly greater than those necessary for fire extinguishing in a closed space (3-5 vol %).

DGC:ST
2 July 70

# Triage of 8(e) Submissions

Date sent to triage: _____ NON-CAP (CAP)

Submission number: 13163A TSCA Inventory: (Y) N D

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Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

(ATOX) SBTOX SEN (w/NEUR)

Group 3 - Elizabeth Margosches (1 copy each)

| | | | | |
|---|---|---|---|---|
| STOX | CTOX | EPI | RTOX | GTOX |
| STOX/ONCO | CTOX/ONCO | IMMUNO | CYTO | NEUR |

Other (FATE, EXPO, MET, etc.): _____

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**entire document:** (0) 1 2 **pages** 19 **pages** _____

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**Contractor reviewer :** JW **Date:** 1/24/96

CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA/ Submission # SEND: 1192 - 13163 SEQ: A

TYPE: INT. SUPP FLWP

SUBMITTER NAME: E. I. Dupont de Nemours and Company

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
0509 REFER TO CHEMICAL SCREENING
0510 CAP NOTICE

VOLUNTARY ACTIONS:
0501 NO ACTION REPORTED
0502 STUDIES PLANNED/UNDERWAY
0503 NOTIFICATION OF WORKERS/USERS
0504 LABELS/MSDS CHANGES
0505 PROCESS/HANDLING CHANGES
0506 APPLIANCE DISCONTINUED
0507 PRODUCTION DISCONTINUED
0508 CONFIDENTIAL

SUB. DATE: 10/18/92 OTS DATE: 11/02/92 CSRAD DATE: 04/24/95

CHEMICAL NAME:
HALON 2402
HALON 1202
HALON 3~~4~~1211

CAS#
124-73-2
75-61-6
353-59-3

75-63-8 → Halon 1301

| INFORMATION TYPE: | | P P C |
|---|---|---|
| 0201 | ONCO (HUMAN) | 01 02 04 |
| 0202 | ONCO (ANIMAL) | 01 02 04 |
| 0203 | CELL TRANS (IN VITRO) | 01 02 04 |
| 0204 | MUTA (IN VITRO) | 01 02 04 |
| 0205 | MUTA (IN VIVO) | 01 02 04 |
| 0206 | REPRO/TERATO (HUMAN) | 01 02 04 |
| 0207 | REPRO/TERATO (ANIMAL) | 01 02 04 |
| 0208 | NEURO (HUMAN) | 01 02 04 |
| 0209 | NEURO (ANIMAL) | 01 02 04 |
| 0210 | ACUTE TOX. (HUMAN) | 01 02 04 |
| 0211 | CHR. TOX. (HUMAN) | 01 02 04 |
| 0212 | ACUTE TOX. (ANIMAL) | 01 02 04 |
| 0213 | SUB ACUTE TOX (ANIMAL) | 01 02 04 |
| 0214 | SUB CHRONIC TOX (ANIMAL) | 01 02 04 |
| 0215 | CHRONIC TOX (ANIMAL) | 01 02 04 |

| INFORMATION TYPE: | | P P C |
|---|---|---|
| 0216 | EPICLIN | 01 02 04 |
| 0217 | HUMAN EXPOS (PROD CONTAM) | 01 02 04 |
| 0218 | HUMAN EXPOS (ACCIDENTAL) | 01 02 04 |
| 0219 | HUMAN EXPOS (MONITORING) | 01 02 04 |
| 0220 | ECOTOX/AQUA TOX | 01 02 04 |
| 0221 | ENV. OCCURRENCE/FATE | 01 02 04 |
| 0222 | EMER INCI OF ENV CONTAM | 01 02 04 |
| 0223 | RESPONSE REQST DELAY | 01 02 04 |
| 0224 | PROD/COMP/CHEM ID | 01 02 04 |
| 0225 | REPORTING RATIONALE | 01 02 04 |
| 0226 | CONFIDENTIAL | 01 02 04 |
| 0227 | ALLERG (HUMAN) | 01 02 04 |
| 0228 | ALLERG (ANIMAL) | 01 02 04 |
| 0229 | METAB/PHARMACO (ANIMAL) | 01 02 04 |
| 0240 | METAB/PHARMACO (HUMAN) | 01 02 04 |

| INFORMATION TYPE: | | P P C |
|---|---|---|
| 0241 | IMMUNO (ANIMAL) | 01 02 04 |
| 0242 | IMMUNO (HUMAN) | 01 02 04 |
| 0243 | CHEM/PHYS PROP | 01 02 04 |
| 0244 | CLASTO (IN VITRO) | 01 02 04 |
| 0245 | CLASTO (ANIMAL) | 01 02 04 |
| 0246 | CLASTO (HUMAN) | 01 02 04 |
| 0247 | DNA DAMAGE/REPAIR | 01 02 04 |
| 0248 | PRODUSE/PROC | 01 02 04 |
| 0251 | MSDS | 01 02 04 |
| 0299 | OTHER | 01 02 04 |

TRIAGE REVIEW

CAS SR

NON-CBI INVENTORY
YES
NO
[illegible]

SCREENING REVIEW
YES (DROP/REFER)
NO (CONTINUE)
REFER

SPECIES
RAT
cat

TOXICOLOGICAL CONCERNS:
LOW Ac, ink
MED
HIGH

USE: Fire-extinguishing agent

PRODUCTION:

[illegible]

13163A

L

Halon 1202: Acute inhalation toxicity in rats is of low concern. A group of ten male Sprague-Dawley rats was exposed to increasing concentrations of the test compound. Clinical signs of toxicity were observed at ≥4,000 ppm and included staggering gait, tremors, cyanosis, narcotic motor paralysis, convulsions, and respiratory distress; 8/10 animals died (1/10 at 30,000 ppm, 1/10 at 38,000 ppm, 2/10 at 39,000 ppm, and 2/10 at 40,000 ppm). The $LC_{50}$ was 40,000 ppm.

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Halon 1211: Acute inhalation toxicity in rats and cats is of low concern based on the results of five studies. In the first three studies, groups of ten male Sprague-Dawley rats were exposed to increasing concentrations of the test compound. In the first study, clinical signs of toxicity were observed at ≥70,000 ppm and included tremors, cyanosis, narcotic motor paralysis, convulsions, and respiratory distress; there were no deaths. In the second study, similar clinical signs were seen at ≥60,000 ppm, and 7/10 animals died (2/10 at 214,000 ppm, 4/10 at 227,000 ppm, and 1/10 after study termination). The results of the third study were comparable to the second study (no details provided). The $LC_{50}$ was 225,000 ppm in rats. In the fourth and fifth studies, a cat was exposed to increasing concentrations of the test compound. In the fourth study, clinical signs of toxicity were observed at ≥41,000 ppm and included pupil dilation, altered behavior (excessive grooming and jerky movements), salivation, ataxia, and convulsions. In the fifth study, clinical signs of toxicity were observed at ≥49,000 ppm and included pupil dilation, altered behavior (excessive grooming and jerky movements), ataxia, and convulsions.

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Halon 1211/1202: Acute inhalation toxicity in rats is of low concern based on the results of three studies. In these studies, groups of ten male Sprague-Dawley rats were exposed to increasing concentrations of the test compound. In the first study, clinical signs of toxicity were observed at ≥53,000 ppm and included tremors, cyanosis, narcotic motor paralysis, convulsions, and respiratory distress; there were no deaths. In the second study, similar clinical signs were seen at ≥65,000 ppm, and 6/10 animals died (1/10 at 183,000 ppm, 3/10 at 204,000 ppm, 1/10 at 210,000 ppm, and 1/10 after study termination). In the third study, similar clinical signs were seen at ≥60,000 ppm, and 6/10 animals died (1/10 at 140,000 ppm, 1/10 at 164,000 ppm, 2/10 at 175,000 ppm, and 2/10 at 180,000 ppm). The $LC_{50}$ was not determined in these studies.

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Halon 2402: Acute inhalation toxicity in rats and cats is of low concern based on the results of six studies. In the first two studies, groups of ten male Sprague-Dawley rats were exposed to increasing concentrations of the test compound. In the first study, clinical signs of toxicity were observed at ≥12,000 ppm and included staggering gait, tremors, cyanosis, narcotic motor paralysis, convulsions, and respiratory distress; 6/10 animals died (2/10 at 57,000 ppm, 2/10 at 58,000 ppm, and 2/10 after study termination). In the second study, similar clinical signs were seen at ≥23,000 ppm, and 8/10 animals died (3/10 at 56,000 ppm and 5/10 at 57,000 ppm). The $LC_{50}$ was 58,000 ppm in rats. In the next four studies, a cat was exposed to increasing concentrations of the test compound. In the third, fourth, and fifth studies, clinical signs of toxicity were observed at ≥5,000 ppm and included head shaking, tremors, ataxia, and convulsions. In the sixth study, clinical signs of toxicity were seen at

≥2,000 ppm and included head shaking, jerky movements, piloerection, ataxia, salivation, and convulsions.